

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IB2004/04405

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, Sequence Search, BIOSIS, PAJ, WPI Data, EMBASE, CHEM ABS Data, LIFESCIENCES, SCISEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| X | "Affymetrix GeneChip Human Genome U95 Set HG-U95A" GENBANK GEO, 11 March 2002 (2002-03-11), XP002293987 see affymetrix probe-set 33799_at, 31625_at, 41680_at, 1239_s_at; 1240_at and 32818_at | 1-7,9-14 |
| L | ----- DATABASE EMBL 'Online! 3 February 2004 (2004-02-03), "Sequence 3748 from Patent W002068579." XP002321904 retrieved from EBI accession no. EM_PAT:CQ717814 Database accession no. CQ717814 L document cited to provide information on the relevant sequence disclosed in WO-A-02068579. the whole document -/- | |

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory, underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

11 May 2005

Date of mailing of the international search report

08/06/2005

Name and mailing address of the ISA

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| C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT | | |
|--|---|-----------------------|
| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| X | <p>-& WO 02/068579 A (PE CORPORATION) 6 September 2002 (2002-09-06) whole document, in particular: claims 1,4,5,8,9,12,13,16 page 12, line 18 - line 34 page 15, line 23 - line 31 page 20, line 5 - page 24, line 7</p> | 1-7,9-16 |
| L | <p>DATABASE EMBL 'Online! 3 February 2004 (2004-02-03), "Sequence 15057 from Patent W002068579." XP002321905 retrieved from EBI accession no. EM_PAT:CQ729123 Database accession no. CQ729123 L document cited to provide information on the relevant sequence disclosed in WO-A-02068579. the whole document</p> | |
| X | <p>-& WO 02/068579 A (PE CORPORATION) 6 September 2002 (2002-09-06) whole document, in particular: claims 1,4,5,8,9,12,13,16 page 12, line 18 - line 34 page 15, line 23 - line 31 page 20, line 5 - page 24, line 7</p> | 1-7,9-16 |
| L | <p>DATABASE EMBL 'Online! 3 February 2004 (2004-02-03), "Sequence 10220 from Patent W002068579." XP002321906 retrieved from EBI accession no. EM_PAT:CQ724286 Database accession no. CQ724286 L document cited to provide information on the relevant sequence disclosed in WO-A-02068579. the whole document</p> | |
| X | <p>-& WO 02/068579 A (PE CORPORATION) 6 September 2002 (2002-09-06) whole document, in particular: claims 1,4,5,8,9,12,13,16 page 12, line 18 - line 34 page 15, line 23 - line 31 page 20, line 5 - page 24, line 7</p> | 1-7,9-16 |
| L | <p>DATABASE EMBL 'Online! 3 February 2004 (2004-02-03), "Sequence 4515 from Patent W002068579." XP002321907 retrieved from EBI accession no. EM_PAT:CQ718581 Database accession no. CQ718581 L document cited to provide information on the relevant sequence disclosed in WO-A-02068579.</p> | |

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------|
| X | -& WO 02/068579 A (PE CORPORATION) 6 September 2002 (2002-09-06) whole document, in particular: claims 1,4,5,8,9,12,13,16 page 12, line 18 - line 34 page 15, line 23 - line 31 page 20, line 5 - page 24, line 7 | 1-7,9-16 |
| X | JANSEN M ET AL: "Molecular classification of tamoxifen-responsive and -resistant breast carcinomas by gene expression profiling." BREAST CANCER RESEARCH AND TREATMENT, vol. 82, no. Supplement 1, November 2003 (2003-11), page S14, XP002321901 & 26TH ANNUAL SAN ANTONIO BREAST CANCER SYMPOSIUM; SAN ANTONIO, TX, USA; DECEMBER 03-06, 2003 ISSN: 0167-6806 the whole document | 17,18 |
| X | PAIK S ET AL: "MULTI-GENE RT-PCR ASSAY FOR PREDICTING RECURRENCE IN NODE NEGATIVE BREAST CANCER PATIENTS-NSABP STUDIES B-20 AND B-14" BREAST CANCER RESEARCH AND TREATMENT, NIJHOFF, BOSTON, US, vol. 82, no. SUPPL 1, 3 December 2003 (2003-12-03), pages S10-S11,ABSTRN, XP001202622 ISSN: 0167-6806 cited in the application the whole document | 17,18 |
| A | STREEKUMAR A ET AL: "USING PROTEIN MICROARRAYS TO STUDY CANCER" BIOTECHNIQUES, EATON PUBLISHING, NATICK, US, no. SUPPL, December 2002 (2002-12), pages 46-53, XP009018820 ISSN: 0736-6205 the whole document | 15,16 |
| A | LOS GERRIT ET AL: "Using mRNA expression profiling to determine anticancer drug efficacy" CYTOMETRY, vol. 47, no. 1, 1 January 2002 (2002-01-01), pages 66-71, XP002321902 ISSN: 0196-4763 page 69, column 1, paragraph 2 - column 2, paragraph 1 | 17,18 |

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------|
| P,A | DOWSETT MITCH: "Biomarker investigations from the ATAC trial: the role of TA01." BREAST CANCER RESEARCH AND TREATMENT. 2004, vol. 87 Suppl 1, 2004, pages S11-S18, XP002321903 ISSN: 0167-6806 ----- | |
| P,A | MA X-J ET AL: "A two-gene expression ratio predicts clinical outcome in breast cancer patients treated with tamoxifen" CANCER CELL, XX, US, vol. 5, no. 6, June 2004 (2004-06), pages 607-616, XP002317299 ISSN: 1535-6108 ----- | |
| T | JANSEN MAURICE P H M ET AL: "Molecular classification of tamoxifen-resistant breast carcinomas by gene expression profiling." JOURNAL OF CLINICAL ONCOLOGY : OFFICIAL JOURNAL OF THE AMERICAN SOCIETY OF CLINICAL ONCOLOGY. 1 FEB 2005, vol. 23, no. 4, 1 February 2005 (2005-02-01), pages 732-740, XP009045184 ISSN: 0732-183X ----- | 1-7,9-18 |

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 8

Claim 8, which is dependent on independent claim 1 relate to a set of marker genes comprising the 44 genes of the 44-gene signature listed in Table 1.

However, no gene is identified in Table 1. In view of the description (e.g. page 3 or page 6, section "44-gene signature"), which indicates that the listing of genes of the 44 gene predictive signature is found in Figure 2, and the fact that Figure 2A and Figure 2B are listing the same 44 genes; claim 8 is interpreted as relating to a set of marker genes comprising the 44 genes of the 44-gene signature listed in Figure 2B.

However, it appears that, at least one of the 44 genes of the 44-gene signature listed in Figure 2B is not clearly defined (Article 6 PCT). In particular, one of the 44 genes defining the 44-gene signature listed in Figure 2B is only identified by its unigene accession number Hs.437986. Said unigene accession number is however deleted from the database. The gene with unigene accession number Hs.437986 is therefore not clearly identified.

Thus, in the absence of a clear and unambiguous definition of all of the 44 genes of the 44-gene signature listed in Figure 2B, no search is performed for claim 8.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

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Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

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2. ☒ Claims Nos.: 8
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; It is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/IB2004/04405

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
|---|---------------------|----------------------------|---------------------|
| WO 02068579 A | 06-09-2002 | WO 02068579 A2 | 06-09-2002 |